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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,748	01/29/2001	Hisashi Narimatsu	1241.17	4282

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,748	NARIMATSU ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-12,17,18,24 and 51-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-12,17,18,24 and 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Prosecution on the merits of this application is reopened on claims 2, 4-18, 24, 51-53 considered unpatentable for the reasons indicated below:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 4 and claims 5-18, 24, 51-53 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2 and 4 recite the phrase "represented by SEQ ID NO...". It is not clear to the Examiner whether the claimed sequences indeed have the said amino acid/nucleotide SEQ IDs because "represented by" can be understood as "to stand for" to symbolize etc. Examiner suggests deletion of said phrase and making a direct reference to the said SEQ ID NO such as "comprising the amino acid sequence SEQ ID NO:1.

Claim 4 and claims 5-18, 24, 51-53 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites the phrase "of a nucleotide sequence represented by SEQ ID NO...". Here again it is not clear whether the claimed nucleotide sequences comprises "the SEQ ID NO:3/4/5". The above phrase opens the claims to nucleotide sequences having insertions, deletions etc., basically to variants.

Therefore, it is not clear whether applicants are claiming variants or the actual sequences in the SEQ ID NO. Examiner suggests deleting the letter "a" and replacing it with "the" such that the phrase reads for example "a DNA having nucleotides 280 to 1194 of the nucleotide sequence SEQ ID NO:3".

Claims 13 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 13 and 15 are drawn to a method of producing the polypeptide comprising the steps of feeding a non-human animal having the recombinant DNA encoding the polypeptide and producing and accumulating said polypeptide "in said medium". It is not clear to the Examiner as to what applicant means by "in said medium". The above phrase lacks antecedence within the claim as well.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected because the invention appears to employ novel vectors. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. §

112 may be satisfied by a deposit of the plasmids. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

In response to the Office action mailed 12-3-02, applicant responded that they have supplied a declaration of their deposit. However, Examiner was unable to find such a record along with said response. Applicant has also not amended the specification updating the deposit information. Therefore the above rejection is maintained.

Claims 2, 4, and claims 5-18, 24, 51-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enzyme with SEQ ID NO:1 or

2 having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure, encoded by the polynucleotide with SEQ ID NO:3, 4, or 5, to vectors and isolated host cells transformed with said vectors and a method of making the polypeptide using said transformed host cells does not reasonably provide enablement for all such enzymes isolated from any source or such enzymes in which one or more amino acids are deleted substituted or added comprising variants, mutants and recombinants and polynucleotides encoding the same, vectors and transgenic non-human animals or plants cells transformed with said vectors and a method of making the polypeptide from such transgenic plants or animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 2, 4, and claims 5-18, 24, 51-53 are so broad as to encompass any alpha 1,3-fucosyltransferase isolated from any source including variants, mutants and recombinants that selectively fucosylates N-acetylglucosamine via alpha 1,3-linkage (see interpretation of phrases

"represented by" etc. under 35 U.S.C. 112, 2nd paragraph) and transgenic non-human animals or plants transformed with said vectors and a method of making the polypeptide from such transgenic plants or animals. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of such enzymes broadly encompassed by the claims and the complex procedures of generating transgenic plants and animals. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single human alpha 1,3-fucosyltransferase and generation of transformed microorganisms as opposed to generating transgenic animals. The only support regarding any genetics of animals or plants involves generating knockout animals which is exactly opposite of generating transgenics. Applicants provide no examples of a transgenic plant or animal which was generated by transfecting the claimed polynucleotides and show the production of the polypeptide from such transgenics.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art

would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Furthermore, it is well known in the art that generating transgenic plants and animals are highly complex and all such generated transgenics may not become successful.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any alpha 1,3-fucosyltransfaase that exhibits the selective property described above because the specification does not establish: (A) regions of the protein structure which may be modified without effecting such activity; (B) the general tolerance of such alpha 1,3-fucosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any alpha 1,3-fucosyltransferase residues with an expectation of obtaining the desired biological function; D) procedures for generating transgenic plants and animals using the claimed polynucleotide and a demonstration of the production of polypeptides from such transgenics; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all such alpha 1,3,-fucosyltransferase or such enzymes with an enormous number of amino acid modifications and furthermore generation of transgenic plants and animals using said polynucleotides. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of alpha 1,3-fucosyltransferases and polynucleotides encoding the same as well as making transgenics having the desired biological characteristics is

unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 2, 4-18, 24, 51-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2, 4-18, 24, 51-53 are directed to polypeptides having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure, polynucleotide encoding the same. Claims 2, 4, and claims 5-18, 24, 51-53 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:1 or 2 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid and fragments and polynucleotides encoding the same, that have not been disclosed in the specification. No description has been provided of all the polypeptide/polynucleotide sequences encompassed by the claims. No information, beyond the characterization of SEQ ID NO:1, 2 and 3-5 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO:1 or 2,

including fragments and variants within the scope of the claimed genus or the structure of polynucleotides encoding the same. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides and the polynucleotides encoding the same are encompassed within the scope of these claims. The specification discloses only two species of the claimed genus of polypeptides and the polynucleotides encoding the same, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

The above rejection has been put in place in view of the revised interpretation of the phrases "represented by". Please see the rejections under 35 U.S.C. 112, 2nd paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 4, and claims 5-12, 17-18, 24, 51-53 are rejected under 35 U.S.C. 102(a) as being anticipated by Ge et al. (J. Biol. Chem. Vol., 272(34):21357-21363, Aug. 1997). This rejection is based upon the public availability of a printed publication. Claims 2, 4, and claims 5-18, 24, 51-53 of the instant application is drawn to an enzyme having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure and variants or mutants of such an enzyme in which one or more amino acids are deleted substituted or and enzymes which are encoded by a polynucleotide which hybridizes under(undefined) stringent conditions to SEQ ID NO:2, 3 or 5, polynucleotides encoding such enzymes, vectors and host cells (transformants) including *E.coli* cells comprising such polynucleotides and methods of making such polypeptide by culturing said host cells as well as method of producing the reaction product of the polypeptide. Claims are also drawn to method of making reaction products using such enzymes. Ge et al. disclose an enzyme with identical properties (see abstract and the entire publication), polynucleotide which encodes such enzymes, vectors and transformants comprising such polynucleotides and method of making such polypeptides and use it in a reaction to make reaction products. Since there is no limitation placed on the number of changes that can be present in the polypeptide or polynucleotide sequence for a variant polypeptide or the hybridizing polynucleotide, above claims read on the enzyme and the DNA sequence disclosed by Ge et al. Thus Ge et al. anticipate claims 2, 4-12, 17-18, 24, 51-53 of this application as written.

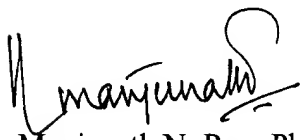
Claims 2, 4-12, 17-18, 24, 51-53 are rejected under 35 U.S.C. 102(b) as being anticipated by Lowe et al. (J. Biol. Chem. Vol., 266(26):17467-17477, Sep. 1991). This rejection is based upon the public availability of a printed publication. Claims 2, 4-12, 17-18, 24, 51-53 of the instant application is drawn to an enzyme having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a non reducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure and variants or mutants of such an enzyme in which one or more amino acids are deleted substituted or and enzymes which are encoded by a polynucleotide which hybridizes under(undefined) stringent conditions to SEQ ID NO:2, 3 or 5, polynucleotides encoding such enzymes, vectors and host cells (transformants) including mammalian cells comprising such polynucleotides and methods of making such polypeptide by culturing said host cells. Claims are also drawn to method of making reaction products using such enzymes. Lowe et al. disclose an enzyme with identical properties (see abstract and the entire publication), polynucleotide which encodes such enzymes, vectors and transformants comprising such polynucleotides including a mammalian cell such as COS-1 and method of making such polypeptides and use said polypeptide in a reaction to make reaction products. Since there is no limitation placed on the number of changes that can be present in the polypeptide or polynucleotide sequence for a variant polypeptide or the hybridizing polynucleotide, above claims read on the enzyme and the DNA sequence disclosed by Lowe et al. Thus Lowe et al. anticipate claims 2, 4-12, 17-18, 24, 51-53 of this application as written.

Here again Examiner notes that the above rejections have been re-instated in view of the revised interpretation of phrases in claims 2 and 4. Amending those claims with a showing of appropriate support in the specification will probably overcome these above rejections.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

January 9, 2006